Schimke immuno-osseous dysplasia

Schimke immuno-osseous dysplasia is a condition characterized by short stature, kidney disease, and a weakened immune system. In people with this condition, short stature is caused by flattened spinal bones (vertebrae), resulting in a shortened neck and trunk. Adult height is typically between 3 and 5 feet. Kidney (renal) disease often leads to life-threatening renal failure and end-stage renal disease (ESRD). Affected individuals also have a shortage of certain immune system cells called T cells. T cells identify foreign substances and defend the body against infection. A shortage of T cells causes a person to be more susceptible to illness.

Other features frequently seen in people with this condition include an exaggerated curvature of the lower back (lordosis); darkened patches of skin (hyperpigmentation), typically on the chest and back; and a broad nasal bridge with a rounded tip of the nose.

Less common signs and symptoms of Schimke immuno-osseous dysplasia include an accumulation of fatty deposits and scar-like tissue in the lining of the arteries (atherosclerosis), reduced blood flow to the brain (cerebral ischemia), migraine-like headaches, an underactive thyroid gland (hypothyroidism), decreased numbers of white blood cells (lymphopenia), underdeveloped hip bones (hypoplastic pelvis), abnormally small head size (microcephaly), a lack of sperm (azoospermia) in males, and irregular menstruation in females.

In severe cases, many signs of Schimke immuno-osseous dysplasia can be present at birth. People with mild cases of this disorder may not develop signs or symptoms until late childhood.

Frequency

Schimke immuno-osseous dysplasia is a very rare condition. The prevalence in North America is estimated to be one in 1 million to 3 million people.

Genetic Changes

Mutations in the *SMARCAL1* gene increase the risk of Schimke immuno-osseous dysplasia. The *SMARCAL1* gene provides instructions for producing a protein whose specific function is unknown. The SMARCAL1 protein can attach (bind) to chromatin, which is the complex of DNA and protein that packages DNA into chromosomes. Based on the function of similar proteins, SMARCAL1 is thought to influence the activity (expression) of other genes through a process known as chromatin remodeling. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during

development. When DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

Mutations in the *SMARCAL1* gene are thought to lead to disease by affecting protein activity, protein stability, or the protein's ability to bind to chromatin. It is not clear if mutations in the *SMARCAL1* gene interfere with chromatin remodeling and the expression of other genes.

The mutations associated with Schimke immuno-osseous dysplasia disrupt the usual functions of the SMARCAL1 protein or prevent the production of any functional protein. People who have mutations that cause a complete lack of functional protein tend to have a more severe form of this disorder than those who have mutations that lead to an active but malfunctioning protein. However, in order for people with *SMARCAL1* gene mutations to develop Schimke immuno-osseous dysplasia, other currently unknown genetic or environmental factors must also be present.

Approximately half of all people with Schimke immuno-osseous dysplasia do not have identified mutations in the *SMARCAL1* gene. In these cases, the cause of the disease is unknown.

Inheritance Pattern

Mutations in the *SMARCAL1* gene are inherited in an autosomal recessive pattern, which means that an increased risk of Schimke immuno-osseous dysplasia results from mutations in both copies of the *SMARCAL1* gene in each cell. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- immunoosseous dysplasia, Schimke type
- Schimke immunoosseous dysplasia
- SIOD

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Schimke immunoosseous dysplasia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0877024/

Other Diagnosis and Management Resources

- GeneReview: Schimke Immunoosseous Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1376

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html
- Health Topic: Dwarfism
  https://medlineplus.gov/dwarfism.html
- Health Topic: Immune System and Disorders
  https://medlineplus.gov/immunesystemanddisorders.html
- Health Topic: Kidney Failure
  https://medlineplus.gov/kidneyfailure.html

Genetic and Rare Diseases Information Center

- Schimke immunoosseous dysplasia
  https://rarediseases.info.nih.gov/diseases/4984/schimke-immunoosseous-dysplasia

Additional NIH Resources

- National Institute of Allergy and Infectious Diseases: Disorders of the Immune System
  https://www.niaid.nih.gov/research/immune-system-research
- National Institute of Diabetes and Digestive and Kidney Diseases: Hyperthyroidism
  https://www.niddk.nih.gov/health-information/endocrine-diseases/primary-hyperparathyroidism

Educational Resources

- Boston Children's Hospital: Kidney Failure
  http://www.childrenshospital.org/conditions-and-treatments/conditions/kidney-failure
- Boston Children's Hospital: Primary Immunodeficiency
  http://www.childrenshospital.org/conditions-and-treatments/conditions/p/primary-immunodeficiency
- MalaCards: schimke immunoosseous dysplasia
  http://www.malacards.org/card/schimke_immunoosseous_dysplasia
- Merck Manual Home Edition for Patients and Caregivers: CChronic Kidney Disease
  http://www.merckmanuals.com/home/kidney-and-urinary-tract-disorders/kidney-failure/chronic-kidney-disease
- National Health Service (UK) Clinical Knowledge Summaries: Chronic Kidney Disease
  http://www.nhs.uk/conditions/kidney-disease-chronic/pages/introduction.aspx
- Orphanet: Schimke immuno-osseous dysplasia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1830

Patient Support and Advocacy Resources

- Human Growth Foundation
  http://hgfound.org/
- International Skeletal Dysplasia Registry, UCLA
  http://ortho.ucla.edu/isdr
- Little People of America
  http://www.lpaonline.org/
- National Kidney Foundation
  https://www.kidney.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/schimke-immuno-osseous-dysplasia/
- The MAGIC Foundation
  https://www.magicfoundation.org/
- University of Kansas Medical Center Resource List: Immune Deficiency Conditions
  http://www.kumc.edu/gec/support/immune.html
- University of Kansas Medical Center: Dwarfism/Short Stature
  http://www.kumc.edu/gec/support/skeldysp.html

GeneReviews

- Schimke Immunoosseous Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1376

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28schimke+immunoosseous+dysplasia%5BTIAB%5D%29+OR+%28schimke+immuno-osseous+dysplasia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- SCHIMKE IMMUNOOSSEOUS DYSPLASIA
  http://omim.org/entry/242900

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